Introduction

Exposure to particulate air pollution has been associated with cardiovascular morbidity and mortality in numerous epidemiologic studies (Brook 2004; Brook et al. 2010; Dockery et al. 1993; Pope and Dockery 2006). Evidence suggests that local traffic is a major source of within-city heterogeneity in air pollution exposures (Bruggé et al. 2007; Clougherty et al. 2008) and that mobile sources of pollution may be an important contributor to adverse health effects (Künzli et al. 2000; Laden 2000; Peters et al. 2004). Several studies focusing specifically on the traffic-related constituents of pollution have reported short-term associations with indicators of cardiovascular health (Delfino et al. 2010a, 2010b; Madrigano et al. 2010; Mordukhovich et al. 2009). Evidence for long-term effects of chronic exposure to traffic-related air pollution has come largely from animal studies, which have demonstrated proatherosclerotic effects of diesel exhaust particles and concentrated ambient urban particles (Chen and Nadziejko 2005; Quan et al. 2010; Sun 2005). Recently, a growing number of epidemiologic studies have also observed associations between subclinical atherosclerosis and estimated fine particulate matter (particulate matter ≤ 2.5 μm in aerodynamic diameter; PM2.5) or distance to major roadway (Bauer et al. 2010; Diez Roux et al. 2008; Hoffmann et al. 2007; Künzli et al. 2005).

Black carbon is a correlate of traffic-related combustion products, and a common surrogate for traffic particles in general, weighted toward diesel vehicles. We have developed a nonlinear land use regression model to estimate black carbon exposures and have applied it within the greater Boston, Massachusetts, metropolitan area (Gryparis et al. 2007). In the present study making use of up to three repeated carotid intima-media thickness (CIMT) measures in a cohort of elderly men, we hypothesized that the estimated annual average concentration of black carbon at participants’ homes in the year before the first study visit would be associated with CIMT, a reliable measure of subclinical atherosclerosis (Kanter et al. 1997; O’Leary and Bots 2010) that predicts cardiovascular outcomes (Nambi et al. 2012; O’Leary et al. 1999). In secondary descriptive analyses, we also estimated associations with residential proximity to a major roadway (defined as U.S. Census feature Class Code A1 (Primary Highway with Limited Access) or A2 (Primary Highway Without Limited Access)) and with average daily traffic within 100 m of residence.

Methods

Study population. The Normative Aging Study is a cohort of community-dwelling men from the greater Boston area recruited in the early 1960s. CIMT was measured in a subsample of participants beginning in 2004, after participants had been followed for four decades. Participants in the CIMT substudy were followed for up to three time points scheduled 1.5 years apart. Our analysis included 380 participants with complete information regarding black carbon concentrations and all covariates at baseline (i.e., the time of the first CIMT measurement). Baseline visits occurred between 2004 and 2008.

CIMT was measured in the anterior region of the common carotid artery using ultrasound (Brook et al. 2010; Diez Roux et al. 2008; Hoffmann et al. 2007; Künzli et al. 2005). In secondary analyses, we estimated differences in annual average black carbon concentration and estimated associations and all covariates at baseline (i.e., the time of the first CIMT measurement). Baseline visits occurred between 2004 and 2008.

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of land use (e.g., cumulative traffic density within 100 m, population density, distance to nearest major roadway, percent urbanization) at a given location. Weather data were obtained from the Boston airport weather station, and planetary boundary layer data from the National Oceanic and Atmospheric Administration’s national reanalysis data set (http://www.esrl.noaa.gov/psd/data/gridded/data.narr.html).

Measurements from continuous ambient monitors and specific monitoring campaigns were used to develop model predictions. We obtained hourly outdoor black carbon concentrations from a total of 12 of these monitors were included in a study of spatial variability in traffic-related pollutant concentrations conducted by the Northeast States for Coordinated Air Use Management (NESCAUM), two sites were operated by the Massachusetts Department of Environmental Protection, and one site was located on the roof of Harvard School of Public Health (HSPH) and operated by the HSPH Department of Environmental Health. Measurements from specific monitoring campaigns came from two sources. First, beginning in 1999, hourly outdoor and indoor black carbon concentrations were measured inside and outside of 30 residential homes, using aethelometers over 48-hr intervals as part of a National Institute of Environmental Health Sciences (NIEHS)–funded study of air pollution and heart rate variability (APAHRV) conducted at HSPH (Zanobetti et al. 2010). Second, 24-hr average outdoor elemental carbon concentrations measured over 7-day periods in 23 locations during the winter and summer of 2000 were obtained from a U.S. Environmental Protection Agency (EPA)–funded multi-pollutant exposures study of sensitive individuals (Brown et al. 2008). We have also incorporated interactions between temporal predictors, such as mixing height and wind speed, and source-based geographic variables, such as traffic density. We used regression
Intima-media thickness and black carbon

Using the near tool in ArcGIS. We classified residential distance to major roadways as 0 to ≤ 100 m, 100 to ≤ 200 m, 200 to ≤ 1,000 m, and > 1,000 m based on prior studies showing that living within 100 m of a major road is associated with cardiovascular events (Tonne et al. 2007), all-cause mortality among myocardial infarction survivors (Rosenbloom et al. 2012), and atherosclerotic progression (Künzli et al. 2010). In addition, living ≤ 200 m of a major road has been associated with coronary artery calcification, another measure of atherosclerotic burden (Hoffmann et al. 2007). Average daily traffic was determined by summing the product of road segment length and estimated annual average daily traffic within a 100-m buffer of the subject’s residence using the MassHighway 2002 Road Inventory database (Massachusetts Department of Transportation 2013). The measures of annual average daily traffic are based on actual traffic counts for major roadways and estimated according to regional traffic for more local roads.

We conducted a separate analysis of CIMT progression (specifically, the change in CIMT from baseline to 3 years after baseline) in association with ln-transformed black carbon at baseline among the 260 participants with a measure of CIMT after 3 years of follow up, adjusting for the baseline values of covariates included in the fully adjusted model.

We also conducted several sensitivity analyses. We examined whether removal of potential confounders and mediators (i.e., statin medication use, total cholesterol, blood pressure medication use, diabetes diagnosis) altered the findings, and we also removed age at baseline from our model because some studies have observed that age is an important confounder and potential effect modifier (Rivera et al. 2013). Next, we explored the exposure–response relationship in fully adjusted models using generalized additive models with penalized splines in R (version 2.13; R Foundation for Statistical Computing, Vienna, Austria). We also estimated the cross-sectional association between black carbon during the year before the first CIMT measurement, and CIMT at the first measurement, with model covariates as defined at baseline. We then restricted analyses to participants whose location of residence did not change during the study and examined associations with a 1-year average exposure to black carbon in 2003 as a surrogate for long-term exposure among this population. The year 2003 was chosen because it is the year before the earliest possible baseline visits. In addition, we estimated the association between black carbon and CIMT after excluding participants who resided outside of the eastern Massachusetts region (approximately within the boundaries of Interstate 495 (I-495); Figure 1) where the original exposure model was developed and tested.
Table 1. Population characteristics [mean ± SD or n (%)] at study center visits (2004–2008) when CIMT was measured.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Visit 1 (n = 380)</th>
<th>Visit 2 (n = 340)</th>
<th>Visit 3 (n = 260)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>75.9 ± 6.4</td>
<td>77.1 ± 6.2</td>
<td>78.0 ± 6.0</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>28.1 ± 4.1</td>
<td>28.2 ± 4.2</td>
<td>28.1 ± 4.2</td>
</tr>
<tr>
<td>Median income (US$)</td>
<td>63,334 ± 20,196</td>
<td>63,360 ± 20,353</td>
<td>64,286 ± 20,858</td>
</tr>
<tr>
<td>Pack-years</td>
<td>17.8 ± 22.7</td>
<td>18.0 ± 22.5</td>
<td>15.9 ± 19.9</td>
</tr>
<tr>
<td>METs (hr/week)</td>
<td>&lt; 12</td>
<td>247 (65)</td>
<td>215 (63)</td>
</tr>
<tr>
<td></td>
<td>12–&lt; 30</td>
<td>81 (21)</td>
<td>74 (22)</td>
</tr>
<tr>
<td></td>
<td>≥ 30</td>
<td>50 (13)</td>
<td>50 (15)</td>
</tr>
<tr>
<td>Education (years)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 12</td>
<td>6 (2)</td>
<td>5 (2)</td>
<td>2 (1)</td>
</tr>
<tr>
<td>12–16</td>
<td>215 (57)</td>
<td>190 (56)</td>
<td>148 (57)</td>
</tr>
<tr>
<td>&gt; 16</td>
<td>159 (42)</td>
<td>145 (43)</td>
<td>110 (42)</td>
</tr>
<tr>
<td>Cholesterol (mg/dL)</td>
<td>174 (37)</td>
<td>173 (37)</td>
<td>170 (34)</td>
</tr>
<tr>
<td>Statin use</td>
<td>208 (55)</td>
<td>202 (59)</td>
<td>162 (62)</td>
</tr>
<tr>
<td>Type 2 diabetes</td>
<td>74 (20)</td>
<td>72 (21)</td>
<td>59 (23)</td>
</tr>
<tr>
<td>≥ 2 Servings of alcohol per day</td>
<td>67 (18)</td>
<td>60 (18)</td>
<td>46 (18)</td>
</tr>
<tr>
<td>CIMT (mm)</td>
<td>0.99 ± 0.18</td>
<td>1.00 ± 0.18</td>
<td>1.01 ± 0.18</td>
</tr>
<tr>
<td>Years since baseline</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>1.6 ± 0.4</td>
<td>3.0 ± 2.2</td>
</tr>
<tr>
<td>Progression since baseline (mm)</td>
<td>0</td>
<td>0.02 ± 0.08</td>
<td>0.04 ± 0.09</td>
</tr>
</tbody>
</table>

Table 2. CIMT percent difference associated with a 1-IQR increase (0.26 µg/m³) in average exposure to black carbon during the year before the first CIMT measurement.

<table>
<thead>
<tr>
<th>Modeling approach</th>
<th>Percent difference (95% CI)</th>
<th>No. of participants</th>
<th>No. of observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parsimonious model (model 1)*</td>
<td>0.9 (0.2, 1.5)</td>
<td>380</td>
<td>977</td>
</tr>
<tr>
<td>Fully adjusted model (model 2)*</td>
<td>1.1 (0.4, 1.7)</td>
<td>378</td>
<td>968</td>
</tr>
<tr>
<td>Sensitivity analyses</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age + other potential mediators removed†</td>
<td>1.2 (0.5, 1.9)</td>
<td>390</td>
<td>976</td>
</tr>
<tr>
<td>Medications and health covariates only*</td>
<td>0.8 (0.2, 1.5)</td>
<td>380</td>
<td>971</td>
</tr>
<tr>
<td>Cross-sectional model†</td>
<td>1.0 (0.3, 1.7)</td>
<td>378</td>
<td>968</td>
</tr>
<tr>
<td>Stable residential address only‡</td>
<td>1.0 (0.3, 1.7)</td>
<td>320</td>
<td>824</td>
</tr>
<tr>
<td>Black carbon in 2003—stable residential address for entire study‡</td>
<td>0.8 (0.2, 1.5)</td>
<td>315</td>
<td>816</td>
</tr>
<tr>
<td>Restriction to region where model was originally built and validated for whole population‡</td>
<td>1.4 (1.3, 4.2)</td>
<td>295</td>
<td>750</td>
</tr>
<tr>
<td>Restriction to region where model was originally built and validated stable residential address for entire study‡</td>
<td>1.9 (1.0, 4.9)</td>
<td>254</td>
<td>646</td>
</tr>
<tr>
<td>Random effect for ZIP code‡</td>
<td>1.1 (0.4, 1.8)</td>
<td>378</td>
<td>968</td>
</tr>
</tbody>
</table>

*Adjusted for age at baseline, BMI, smoking status (never, current, former), time since baseline (days). †Adjusted for model 1 covariates + statin medication use, total cholesterol, systolic blood pressure, blood pressure medication use, and diabetes diagnosis, pack-years smoked, level of education, ≥ 2 servings of alcohol per day, physical activity (METs per week: 0 < 12.12 to < 30, ≥ 30 hr), and U.S. Census tract-level median income. ‡Adjusted for BMI, pack-years smoked, smoking status, education status, ≥ 2 servings of alcohol per day, median income, time since study baseline. ††Adjusted for age at baseline, BMI, pack-years smoked, statin use, blood pressure medications, smoking status, diabetes diagnosis, adjusted exam date, systolic blood pressure, and total cholesterol. *Adjusted for age at baseline, BMI, pack-years smoked, statin use (yes/no), blood pressure meds (yes/no), smoking status (never, current, former), education status (< 12 years, 12–16, > 16 years), ≥ 2 servings of alcohol per day, median income at the census tract level, diabetes (yes/no), time since study inception, systolic blood pressure, and cholesterol. Adjusted for model 2 covariates.

Table 3. Model 2 results stratified by potential susceptibility factors according to potential effect modifiers at baseline.

<table>
<thead>
<tr>
<th>Stratification factor</th>
<th>Category</th>
<th>Percent difference (95% CI)</th>
<th>Penetration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>≤ 75 years</td>
<td>0.9 (–0.04, 1.7)</td>
<td>0.33</td>
</tr>
<tr>
<td></td>
<td>&gt; 75 years</td>
<td>1.5 (0.6, 2.5)</td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td>≤ 12 years</td>
<td>1.1 (0.1, 2.0)</td>
<td>0.75</td>
</tr>
<tr>
<td></td>
<td>&gt; 12 years</td>
<td>1.1 (0.2, 2.0)</td>
<td></td>
</tr>
<tr>
<td>Statin use</td>
<td>No</td>
<td>1.2 (0.2, 2.2)</td>
<td>0.97</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>0.9 (0.2, 1.7)</td>
<td></td>
</tr>
<tr>
<td>BMI &gt; 30</td>
<td>No</td>
<td>1.4 (0.7, 2.2)</td>
<td>0.04</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>0.6 (0.6, 1.8)</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>No</td>
<td>1.1 (–0.4, 1.7)</td>
<td>0.28</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>0.9 (1.1, 1.9)</td>
<td></td>
</tr>
</tbody>
</table>

At first visit, there were 213 individuals > 75 years of age (p = 0.33), 96 obese individuals (p = 0.04), 241 participants with education beyond high school (p = 0.75), 208 using statins (p = 0.97), and 74 with diabetes (p = 0.28).

We also considered clustering by socioeconomic status by including an additional random effect for ZIP code. In secondary descriptive analyses, we estimated associations between CIMT and residential proximity to a major roadway (0 to ≤ 100 m, > 100 to ≤ 200 m, > 200 to ≤ 1,000 m, or > 1,000 m) and between CIMT and average daily traffic within 100 m of the participant’s residence (categorized according to quartiles).

Results

A total of 380 participants completed a baseline visit between 2004 and 2008, including 340 (89%) who completed at least two follow-up visits and 260 (68%) who completed three follow-up visits through 2010 (Table 1). At baseline (the time of first CIMT measurement), the mean (± SD) age and BMI of participants were 75.9 ± 6.4 years and 28.1 ± 4.1 kg/m² respectively, and 355 (93%) were retired or semi-retired. The mean CIMT at baseline was 0.99 ± 0.18 mm, which was higher than levels observed in younger, population-based cohorts. Participants were 61 to 96 years of age at median baseline and CIMT ranged from 0.63 to 2.10. Median predicted black carbon concentrations at baseline for each subject was 0.29 µg/m³, with the interquartile range (IQR) equivalent to 0.26 µg/m³ (25th to 75th percentile, 0.16–0.42 µg/m³).

Based on our fully adjusted model, an IQR increase in annual average black carbon during the year before baseline was associated with a 1.1% (95% CI: 0.4, 1.7%) higher CIMT, consistent with a 0.01-mm increase from the mean CIMT of 0.99 mm at baseline (Table 2), which was similar to the mean rate of progression per year in this population (i.e., 0.01 mm). This association was stronger than estimated by the parsimonious model (0.9% higher; 95% CI: 0.2, 1.5%) adjusted for age, BMI, smoking, and time since baseline only.

p-Values for cross-product terms indicated a statistically significant interaction (p < 0.05) for BMI only (Table 3). Specifically, the association between an IQR increase in black carbon and CIMT was stronger among men who were not obese at baseline (1.4%; 95% CI: 0.7, 2.2%; n = 284) than among men who were obese (0.6%; 95% CI: −0.6, 1.8%; n = 96). Interaction results were observed. CIMT progression among the 260 men with CIMT measured 3 years apart was not significantly associated with an IQR increase in annual average black carbon at baseline (−0.0002 mm decrease from baseline on average; 95% CI: −0.002, 0.001 mm; p = 0.79).

In our sensitivity analyses (Table 2), point estimates did not change when we removed additional potential mediators associated with health status. Results from our cross-sectional...
analysis restricted to first measure of CIMT produced similar estimates to those observed in our final model. We did not observe any deviation from linearity on the log scale. In analyses in which we excluded participants who changed their residence during the study \((n = 60, 16\%)\), results were similar to final models. Examining the association among individuals with stable residence since 2003 produced similar, slightly attenuated estimates. A 2.4-fold difference in exposure in 2003 (median = 0.30 µg/m³, IQR = 0.19–0.46) was associated with 0.8% higher CIMT (95% CI: 0.1, 1.5%). In analyses in which we additionally excluded individuals with addresses outside the region in which the model was originally developed and tested, point estimates were stronger but did not meet statistical significance because of the reduction in sample size. Inclusion of the random effect for ZIP code did not materially change the results from the full model [1.1% higher CIMT (95% CI: 0.4, 1.8%)].

In descriptive analyses, we estimated associations between residential proximity to an A1 or A2 roadway and average daily traffic within 100 m of home address at baseline. Because there were only 10 participants living < 100 m from a major road, we collapsed the ≤ 100-m and 100- to ≤ 200-m categories. In comparison to living > 1,000 m from a major road, living < 200 m or 200–1,000 m away was associated with –1.4% (95% CI: –7.11, 4.6%) or –2.2% lower CIMT (95% CI: –5.7, 1.5%), respectively. For the average daily traffic, we estimated associations by quartiles of exposure (7,795–212,923; 212,924–416,029; 416,030–1,251,886; and 1,251,887–9,861,107 vehicles/day). Compared with living in a location in the lowest quartile of exposure, living in a location with average daily traffic in the second, third, or fourth quartile of exposure was associated with 4.6% higher (95% CI: –0.3, 9.6%), 4.3% higher (95% CI: –0.5, 9.3%), or 2.7% (95% CI: –2.0, 7.6%) higher CIMT, respectively.

**Discussion**

We observed a positive association between average black carbon exposure at the home address during the year before baseline and subsequent subclinical atherosclerosis measured by CIMT. A major feature of this study is the use of modeled black carbon at home address; black carbon is a more specific marker for traffic particles than PM₂.₅ and one which can show considerable spatial heterogeneity within distances of a few hundred meters. Our findings are consistent with prior studies from cross-sectional analyses of CIMT and PM₂.₅ exposures among participants in Los Angeles, California (Künzli et al. 2005); the Multi-Ethnic Study of Atherosclerosis (MESA) (Diez Roux et al. 2008), which used 20-year estimates of modeled exposure; and 1-year averaged modeled exposure from the Heinz-Nixdorf Recall study in Germany (Bauer et al. 2010) in addition to a recent study that reported associations with NO₂ (nitrogen dioxide), which is also a marker of traffic particles (Rivera et al. 2013).

Previous studies have reported that CIMT is a strong predictor of future vascular events. A meta-analysis reported that age- and sex-adjusted relative risks of myocardial infarction and stroke per 0.10 mm CIMT difference were 1.15% (95% CI: 1.12, 1.17%) and 1.18% (95% CI: 1.16, 1.21%), respectively; and although the relationship between CIMT and risk was not linear, linear models fit well for moderate-to-high CIMT levels. The levels of CIMT at baseline observed for men who participated in our study were higher than those reported in populations that included younger, healthier populations of both men and women (Chambless et al. 1997; Lim et al. 2008) and were more similar to those reported in a study of patients with arterial disease and cardiovascular risk factors (Dijk et al. 2006). In the Atherosclerosis Risk in Communities (ARIC) study, a cutoff of 1 mm was used to evaluate risk of coronary heart disease, and the hazard ratio for coronary heart disease comparing men with CIMT measures ≥ 1 mm versus < 1 mm was 1.85 (95% CI: 1.28, 2.69), which would suggest that the levels of CIMT observed in our study population might be associated with elevated risk of cardiovascular disease.

A few recent studies have begun to examine associations between ambient air pollution exposure and atherosclerotic progression as measured by CIMT. In one recent study, both PM₂.₅ and residential distance from highway were examined in a population of participants pooled from five double-blind randomized trials that estimated the effects of interventions on the progression of CIMT in the Los Angeles area (Künzli et al. 2010). Künzli et al. (2010) observed a rate of progression of 5.46 µm/ year associated with living within 100 m of major road and that a 10-µg/m³ increase in PM₂.₅ was associated with a slightly smaller change of 2.53 (95% CI: –0.31, 5.38) µm/year for men and women. More recently, similar results have been reported in MESA, where Adar et al. (2013) observed that 2.5-µg/m³ higher residential PM₂.₅ during the follow-up period was also associated with a 5.0 µm/year (95% CI: 2.6, 7.4 µm/year) greater IMT progression among persons in the same metropolitan area. We did not observe a significant association with progression over 3 years; given the relatively short period of follow-up on only 260 participants, we had limited power to test this association in the present study. In addition, men who survived long enough to participate in the present study may have had a low likelihood of CIMT progression, and healthier participants within the cohort may have been more likely to have completed follow-up than men with increasing CIMT. The annual rate of CIMT progression in our study population (approximately 0.01 mm, or 10 µm/year) was similar to rates reported in MESA and other cohort studies including the ARIC study (Ranjit et al. 2006) and in older men and women in the Whitehall II study (Halcox et al. 2009).

We observed significant associations with the mean of in-transformed daily predictions of black carbon at participant residence. In our secondary, exploratory analyses, we examined associations with measures of residential proximity to major roadways as well as traffic density. In the present study, contrary to our expectation, mean CIMT was greatest in men living farthest from a major road at baseline, although associations were not statistically significant and only a small number of participants (n = 32) lived ≤ 200 m from a major road at baseline. A study by Allen et al. (2009) reported no association between residential proximity to a major roadway and aortic artery calcification, another measure of atherosclerotic burden. As these authors have pointed out, the roadway classification system describes a type of road and not the traffic volume and traffic pollution, more directly, which may in part explain these differing results. In the present study, CIMT was higher in participants exposed to traffic counts higher than the first quartile, but estimates were relatively imprecise and not statistically significant.

Of the potential susceptibility factors that we examined, the only statistically significant interaction was observed for stratification by obesity: We observed higher associations with black carbon among non-obese individuals. We hypothesized that this finding was due to the strong association between BMI and CIMT in this study, such that obesity and other related factors likely have a larger effect on a measure of subclinical atherosclerosis than black carbon and the association between black carbon and intima-media thickness is observed only in the non-obese individuals. In addition, Freedman et al. (2004) have noted that CIMT may be more difficult to measure in obese individuals and may be assessed with less precision. The association between black carbon and CIMT was also somewhat stronger in men without diabetes than in men with diabetes, although estimates were imprecise. These results contrast those of other studies that have reported evidence to suggest that persons with diabetes are particularly susceptible to the effects of traffic pollution (Baja et al.
To attempt to address this, we also analyzed
not fully account for long-term time trends.
between 2004 and 2008 and, therefore, may
black carbon concentrations estimated for
only. In addition, our analysis of annual black
had considerably less power to detect an asso-
cially significant. It is possible, however, that
CIMT, but results were no longer statisti-
ces examinations between black carbon levels and
levels of exposure outside the region within
were imprecise and the CIs were
very low exposure values. Whereas our model
diagnoses suggested that the association was
linear on the log scale, results from analy-
examining the association on the natu-
ral scale suggested a nonlinear dose response
and a negative slope at high levels, although
these results were imprecise and the CIs were wide.
Our black carbon model predicts lower levels of exposure outside the region within I-495, in which it was originally developed.
Although we had considerably less power to
detect an association in analyses restricted to
within I-495 only (77% of participants), in these analyses we estimated stronger associa-
tions between black carbon levels and CIMT, but results were no longer statisti-
cally significant. It is possible, however, that
the estimates we report in the full population underestimate the true association because of exposure misclassification, although we had considerably less power to detect an associa-
tion in analyses restricted to within I-495 only. In addition, our analysis of annual black carbon concentrations may not fully account
for long-term time trends because they were based on associations with annual average black carbon concentrations estimated for
the year prior to baseline, which occurred between 2004 and 2008 and, therefore, may
not fully account for long-term time trends. To attempt to address this, we also analyzed
the associations assigning everyone black car-
bon exposure based on 2003 data for their
addresses and the results were similar to those
observed in our final model. Future work will
be necessary to elucidate this association.
Because our study participants were
elderly male residents of the Boston area, 97% of whom reported their race as white,
these results may not be generalizable to other
populations of environmentally exposed men
and women. This particular analysis was also limited to a subset of Normative Aging
Study participants who continued to be
followed during the study period, many of
whom consented to return on an additional
day for CIMT testing. Our study participants
were elderly men ranging in age from 61 to
96 years of age at first visit, who, on aver-
age, had already developed a considerable
degree of atherosclerotic burden at baseline.
Furthermore, the mean CIMT reported at
baseline was higher than has been reported in
other community-based samples, which
generally have younger participants (Adar
et al. 2013; Nett et al. 2013). There may be
some degree of measurement error in CIMT,
but this would likely be nondifferential with
respect to exposure. In addition, we also
cannot rule out the role of residual confounding
by socioeconomic position or other factors.
Although there was some attrition over time,
two or more measurements were obtained for
89% of individuals.

Conclusions
We observed that low levels of ambient expo-
sure to estimated black carbon were associ-
ated with CIMT in a population of elderly
men continuing to participate in a long-term
prospective cohort study. Given the grow-
ing interest in the relationship between air
pollution and atherosclerosis (Künzli et al.
2011) and the limited body of human studies
examining repeated measurement of indica-
tors of atherosclerotic burden, future studies
are needed to substantiate the association between specific sources of pollution and
atherosclerotic progression in order to clarify
the underlying mechanisms.

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